Dec. 10, 1947.

Dear Ed-

The genetic aspects of the carbohydrase mutation program concerning which I have written before have come to a head and have to wait now for the chemistry to catch up. It may be a long wait, firstly to mull over the possible approaches, and secondly because I am not to well equipped as yet (e.g. Warburgs).

The genetical fact is that Y-53 and W-45 which are both Lactose-negative, the one in T-L-B_1- stock, the other in B-M-, recombine to give a fairly large proportion (20-30%) lactose-positive prototrophs. The obvious loopholes have been checked, and the experiments repeated, so that in my mind there is little doubt that mutation at either one of two loci yields the lactose-negative phenotype. The finally tack in the coffin, demonstrating the recovery of the double-Lac- mutant is being sought now. The locus of Lac_1 is as shown on the published map. Lac_2 is between BM and Lac_1, only a few units from BM. The smoke about phenyl galactoside utilization is due to there being two Lac loci, and hasn't been entirely cleared up , but seems to be controlled by only one of these loci.

The chemical problem is: how many enzymes can there be in bringing lactose into the common pathway of carbohydrate metabolism. The preponderance of evidence for coli seems to be that there is a simple lactase which hydrolyses lactose. Even if the pathway were phosphorolystic, there need be but a single step. But most important, how to prove whether there is one or more than one enzyme involved. The rub is that lacto-zymase is adaptive, so that any enzymatic block along the way, by preventing the utilization of the carbohydrate, could prevent the formation of all the other enzymes. For this reason, mixed-juice or mixed resting cells might be inconclusive, but they haven't been done yet. If you have any ideas on the subject, let me know. Another thing that has to be done is to straighten out the phenyl-galactoside story, there might be a lead there.

Starting with a successful accident, I am leaving minerals out of the minimal medium now. If anything they grow better than with them in. I got no response of Y-132 to glycine + arginine. The glycine tube finally adapted, but this is not a growth response. I'll run it down again along with a batch of Y-120 doubles I've been picking up.

Please keep the lactose story entre-nous, or at least within OBL for a while. It's too early to be sounding taps to the 1:1 theory.

Sincerely,